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Impact of Intravenous Beta-Blockade Before Primary Angioplasty on Survival in Patients Undergoing Mechanical Reperfusion Therapy for Acute Myocardial Infarction

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OBJECTIVES We sought to examine the effect of intravenous beta-blockers administered before primary percutaneous coronary intervention (PCI) on survival and myocardial recovery after acute myocardial infarction (AMI).

BACKGROUND Studies of primary PCI but not thrombolysis have suggested that beta-blocker administration before reperfusion may enhance survival. Whether oral beta-blocker use before admission modulates this effect is unknown.

METHODS The Controlled Abciximab and Device Investigation to Lower Late Angioplasty Complications (CADILLAC) trial randomized 2,082 AMI patients to either stenting or balloon angioplasty, each ± abciximab. In accordance with the protocol, intravenous beta-blockers were administered before PCI in the absence of contraindications.

RESULTS A total of 1,136 patients (54.5%, BB+ group) received beta-blockers before PCI, whereas 946 (45.5%, BB− group) did not. The 30-day mortality was significantly lower in the BB+ group than in the BB− group (1.5% vs. 2.8%, p = 0.03), an effect entirely limited to patients who had not been receiving beta-blockers before admission (1.2% vs. 2.9%, p = 0.007). In contrast, no survival benefit with pre-procedural beta-blockers was observed in patients receiving beta-blockers at home (3.3% vs. 1.9%, respectively, p = 0.47). By multivariate analysis, pre-procedural beta-blocker use was an independent predictor of lower 30-day mortality among patients without previous beta-blocker therapy (relative risk = 0.38 [95% confidence interval 0.17 to 0.87], p = 0.02). The improvement in left ventricular ejection fraction from baseline to seven months was also greater after intravenous beta-blockers (3.8% vs. 1.3%, p = 0.01), an effect limited to patients not receiving oral beta-blockers before admission.

CONCLUSIONS In patients with AMI undergoing primary PCI, myocardial recovery is enhanced and 30-day mortality is reduced with pre-procedural intravenous beta-blockade, effects confined to patients untreated with oral beta-blocker medication before admission. (J Am Coll Cardiol 2004;43:1780–7) © 2004 by the American College of Cardiology Foundation

Despite advances in reperfusion therapy for acute myocardial infarction (AMI), a significant proportion of patients still develop recurrent ischemia, reinfarction, and malignant

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ventricular arrhythmias, and/or they die. Whether prophylactic intravenous beta-adrenergic blocker therapy before reperfusion improves survival is undetermined. Historically, several studies demonstrated reduced mortality in patients treated with intravenous beta-blockers in AMI without reperfusion therapy (1–3). Conversely, trials of intravenous beta-blockers in patients treated with thrombolytic therapy, while demonstrating reductions in recurrent ischemia, have reported either no survival benefit (4,5) or increased mortality (6). A recent report from the Primary Angioplasty in Myocardial Infarction (PAMI) trials found intravenous beta-blocker administration before percutaneous coronary intervention (PCI) to be associated with improved in-hospital survival and reductions in procedural complications, including serious arrhythmias and the need for intra-aortic balloon counterpulsation (7).

To confirm and further explore the early and late benefits of intravenous beta-blocker administration before primary PCI, we examined the database from a large, prospective,

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Abbreviations and Acronyms

AMI	= acute myocardial infarction
CADILLAC	= Controlled Abciximab and Device Investigation to Lower Late Angioplasty Complications
CI	= confidence interval
HR	= hazard ratio
LVEF	= left ventricular ejection fraction
PAMI	= Primary Angioplasty in Myocardial Infarction
PCI	= percutaneous coronary intervention
TIMI	= Thrombolysis In Myocardial Infarction

multicenter, randomized study of mechanical reperfusion in AMI, the Controlled Abciximab and Device Investigation to Lower Late Angioplasty Complications (CADILLAC) trial. Moreover, we hypothesized that the utility of these agents would be most evident in or confined to those patients not maintained on oral beta-blocker therapy before admission.

METHODS

Details of the CADILLAC trial have been previously reported (8). Briefly, 2,082 patients ≥18 years of age with AMI and symptom onset within 12 h undergoing primary PCI were randomized to primary balloon angioplasty versus Multilink stent implantation, each ± abciximab. The principal clinical exclusion criterion was cardiogenic shock. Angiographic inclusion criteria required eligibility for stent implantation, including a native coronary artery culprit vessel with reference diameter 2.5 to 4.0 mm and lesion length ≤64 mm. By protocol, intravenous beta-blockers (e.g., metoprolol 5 mg intravenously over 2 min, given every 5 min up to 3 doses) were strongly recommended before catheterization or intervention, in the absence of clinical contraindications. Detailed information on medication usage was collected at the time of admission, in the emergency room, in the catheterization suite, during the hospitalization, at discharge, and during the clinical follow-up periods of 1, 6, and 12 months. For the purpose of the current analysis, pre-procedural beta-blocker use was defined as any in-hospital administration of a beta-blocker before arrival in the catheterization laboratory or before balloon inflation.

End points and statistical analysis. The primary end point was a composite of major adverse cardiac events, defined as death from any cause, reinfarction, repeat target vessel revascularization as a result of ischemia, or disabling stroke. The components of the composite end point have been previously defined (8). Severe hypotension before PCI was defined as systolic blood pressure <90 mm Hg for >30 min or requiring pressor therapy. Severe bradyarrhythmia before PCI was defined as asystole or bradycardia requiring atropine or pacing. Quantitative coronary angiography and ventriculographic assessment were performed using dedicated software (QCA-CMS, MEDIS, Leiden, the Netherlands) at an independent core angiographic laboratory at the Cardiovascular Research Foundation in New York (8). Antegrade coronary blood flow was evaluated using the Thrombolysis In Myocardial Infarction (TIMI) scale (9). Left ventricular ejection fraction (LVEF) was calculated using the length-area method (10), and regional wall motion was calculated using the centerline chord method (11).

Categorical data were compared using the Fisher exact test. Continuous variables are presented as medians and interquartile ranges and were compared using the Kruskal-Wallis non-parametric test. Clinical outcomes are presented as Kaplan-Meier survival estimates and were compared using the log-rank test. Independent predictors of survival were determined with Cox proportional hazard regression analysis using stepwise selection of correlative univariate clinical and angiographic parameters with entry and exit criteria of $p < 0.1$. Independent predictors of improvement in LVEF from baseline to follow-up were determined by multiple linear regression using stepwise selection with entry and exit criteria of $p < 0.1$. All baseline variables in Table 1 were available for selection in these models, along with stent and abciximab randomization and pre-procedural intravenous beta-blocker use. For all analyses, a two-sided $p < 0.05$ was considered statistically significant.

RESULTS

Baseline characteristics. Pre-procedural beta-blockers were administered in 1,136 (54.5%) patients (BB+ group) and were not given to the remaining 946 patients (45.5%, BB− group). As seen in Table 1, pre-procedural beta-blocker therapy was more frequently administered at U.S. sites than non U.S. sites. The BB+ patients were younger and less frequently had pre-existing renal failure, previous AMI, or previous PCI but were more likely to have hypertension and anterior infarction with depressed global and regional left ventricular function. TIMI flow grade 3 at baseline angiography was present in slightly more patients who received pre-procedural beta-blockers than in those who did not, and symptom onset to first balloon inflation was slightly longer with pre-procedural beta-blocker use.

Pre-procedural beta-blocker therapy and clinical outcomes. Clinical outcomes during PCI and throughout the index hospitalization are shown in Table 2. New onset congestive heart failure in the catheterization laboratory was slightly more frequent in patients treated with pre-procedural beta-blockers. Stent and abciximab use and final procedural success rates, including TIMI flow grade 3 achieved and luminal dimensions, were similar in the BB+ and BB− groups. In-hospital mortality was significantly lower and the length of hospitalization shorter among BB+ than among BB− patients (Table 2). Patients receiving pre-procedural beta-blockers were more likely to be discharged receiving statins, angiotensin-converting inhibitors, and oral beta-blockers.

At 30 days, mortality was significantly reduced in BB+

Table 1. Baseline Characteristics of Patients Stratified by Pre-Procedural Beta-Blocker Therapy

	BB+ Group (n = 1,136)	BB− Group (n = 946)	p Value
Clinical features			
U.S. site (%)	90.9	70.8	0.0001
Age (yrs)	58.0 (49.0, 67.0)	62.0 (52.0, 70.0)	0.0001
Male gender (%)	72.9	73.2	0.92
Diabetes mellitus (%)	17.3	15.9	0.40
Current smoker (%)	43.9	42.2	0.42
Hypercholesterolemia (%)	38.0	37.7	0.93
Hypertension (%)	50.2	45.6	0.04
Previous myocardial infarction (%)	11.8	16.0	0.006
Previous coronary angioplasty (%)	9.5	13.2	0.008
Renal insufficiency (CrCl <60 ml/min)	15.4	21.3	0.0009
Chest pain to first balloon inflation (hr)	4.2 (3.0, 6.5)	3.8 (2.7, 5.7)	0.0001
Killip class 2 or 3 (%)	10.5	11.3	0.62
Pre-admission medications			
Aspirin (%)	26.6	27.9	0.52
Beta-blockers (%)	13.5	16.4	0.06
Statins (%)	12.5	11.2	0.38
Calcium blockers (%)	15.0	16.2	0.47
ACE inhibitors/ARB (%)	10.2	8.5	0.18
Thienopyridines (%)	1.9	3.4	0.052
Angiographic features			
Three-vessel disease (%)	15.4	15.8	0.86
Infarct vessel = left anterior descending (%)	42.3	30.0	0.0001
Reference vessel diameter (mm)	2.95 (2.6, 3.3)	2.95 (2.6, 3.3)	0.35
Diameter stenosis (%)	100 (74.1, 100)	100 (76.3, 100)	0.052
TIMI flow grade 3 (%)	23.8	20.0	0.04
Left ventricular ejection fraction (%)	54.3 (46.1, 62.1)	57.7 (48.9, 64.3)	0.0001
Infarct zone regional wall motion (SD/chord)	−1.37 (−1.68, −0.89)	−1.24 (−1.61, −0.82)	0.007

Continuous variables are expressed as median, with interquartile range in parentheses.
ACE = angiotensin-converting enzyme; ARB = angiotensin receptor blockers; BB = beta-blocker; CrCl = creatinine clearance; SD = standard deviation; TIMI = Thrombolysis In Myocardial Infarction.

patients compared with BB− patients (Fig. 1). The absolute risk reduction in 30-day mortality with pre-procedural beta-blocker therapy was 1.7%, corresponding to a hazard ratio (HR) of 0.52 (95% confidence interval [CI] 0.28 to 0.95). There were no differences, however, in the 30-day rates of reinfarction (0.8% vs. 0.9%, p = 0.88), target vessel revascularization (3.4% vs. 3.5%, p = 0.84), or disabling stroke (0.2% vs. 0.1%, p = 0.68) in the BB+ and BB− groups, respectively.

At one year, the absolute risk reduction in mortality in the BB+ compared with the BB− group was 1.2% (Fig. 1), though with increasing mortality in both groups this was no longer significant (HR = 0.74 [95% CI 0.49 to 1.12], p = 0.15).

Impact of pre-hospital oral beta-blocker therapy. The effect of pre-procedural intravenous beta-blocker administration on 30-day survival was strongly influenced by routine oral beta-blocker use before admission, as depicted in Figure 2. Pre-procedural beta-blocker administration markedly reduced 30-day mortality in patients not maintained on this class of agents at home (from 2.9% to 1.2%, HR = 0.40 [95% CI 0.20 to 0.80], p = 0.007), whereas patients taking oral beta-blocker therapy did not benefit by pre-procedural intravenous beta-blocker administration (30-day mortality 3.3% vs. 1.9% in the BB− group, HR = 1.68 [95% CI 0.40 to 7.00], p = 0.47). By multivariate analysis, pre-procedural beta-blocker administration was an independent predictor of 30-day survival in patients not taking beta-blockers before admission (Table 3).

Paired left ventriculograms were available at baseline and at protocol-specified seven-month angiographic follow-up for 230 and 233 patients in the BB+ and BB− groups, respectively. Baseline LVEF was lower in BB+ patients, though seven-month follow-up LVEF was similar in both groups, corresponding to a significantly greater incremental improvement in LVEF in the BB+ group compared with the BB− group (Fig. 3). The increase in LVEF from baseline to follow-up in the BB+ group was most pronounced in patients not taking oral beta-blockers before admission. In patients maintained on beta-blockers before admission, the change in LVEF was similar in BB+ and BB− patients. By multiple linear regression, pre-procedural intravenous beta-blocker administration in patients not receiving oral beta-blockers before admission was an independent predictor of greater increase in LVEF from baseline to seven-month follow-up (beta coefficient = 3.24, p < 0.0001).

Analyses excluding patients with hemodynamic and electrical instability before catheterization. Compared with BB+ patients, BB− patients were slightly more likely to

Table 2. Catheterization Laboratory and In-Hospital Outcomes

	BB+ Group (n = 1,136)	BB− Group (n = 946)	p Value
Interventional strategy			
Stent implanted (%)	56.1	57.6	0.50
Abciximab administered (%)	52.2	54.2	0.38
Catheterization laboratory complications			
Heart failure not present on admission (%)	1.1	0.3	0.05
Use of intra-aortic balloon pump (%)	0.1	0.5	0.10
Serious arrhythmia* (%)	5.4	5.9	0.63
Cardioversion (%)	0.5	0.1	0.13
Defibrillation (%)	1.1	0.7	0.49
Cardiopulmonary resuscitation (%)	0.0	0.1	0.99
Intubation (%)	0.4	0.5	0.73
Final results			
TIMI flow grade 3 (%)	96.1	95.0	0.28
Reference vessel diameter (mm)	2.97 (2.63, 3.34)	2.99 (2.64, 3.38)	0.20
In-lesion minimal luminal diameter (mm)	2.25 (1.94, 2.59)	2.25 (1.95, 2.60)	0.49
In-lesion diameter stenosis (%)	18.1 (9.2, 27.0)	17.9 (8.7, 27.3)	0.79
In-hospital results			
Mortality (%)	1.1	2.2	0.057
Length of stay (days)	3.3 (2.8, 4.7)	3.9 (2.8, 6.0)	0.001
Discharge medications			
Aspirin (%)	96.8	96.6	0.91
Beta-blockers (%)	85.8	70.8	0.0001
Statins (%)	32.8	25.7	0.0005
Calcium blockers (%)	4.6	5.6	0.31
ACE inhibitors/ARB (%)	36.8	32.4	0.04
Thienopyridines (%)	67.1	67.9	0.74

*Arrhythmia requiring medication, electrical intervention, or cardiopulmonary resuscitation.
Abbreviations as in Table 1.

present with severe hypotension and/or bradyarrhythmias (2.4% vs. 0.7%, p = 0.001, and 7.1% vs. 2.7%, p = 0.0001, respectively). Therefore, analyses were also performed after the exclusion of the 118 patients with these confounding conditions. In this cohort (n = 1,964), a trend towards reduced 30-day mortality was observed in BB+ compared with BB− patients (1.4% vs. 2.3%, HR = 0.56 [95% CI 0.29 to 1.08], p = 0.08). Among patients without preadmission oral beta-blocker therapy, 30-day mortality was significantly lower in BB+ compared with BB− patients (1.1% vs. 2.5%, HR = 0.40 [95% CI 0.19 to 0.86], p = 0.001). Among patients receiving oral beta-blocker therapy before admission, however, 30-day mortality was not significantly different in BB− versus BB+ patients (3.4% vs. 1.5%, respectively, HR = 2.27 [95% CI 0.44 to 11.72], p = 0.31). By multivariate analysis, intravenous beta-blocker therapy remained an independent correlate of improved survival in patients previously untreated with beta-blockers

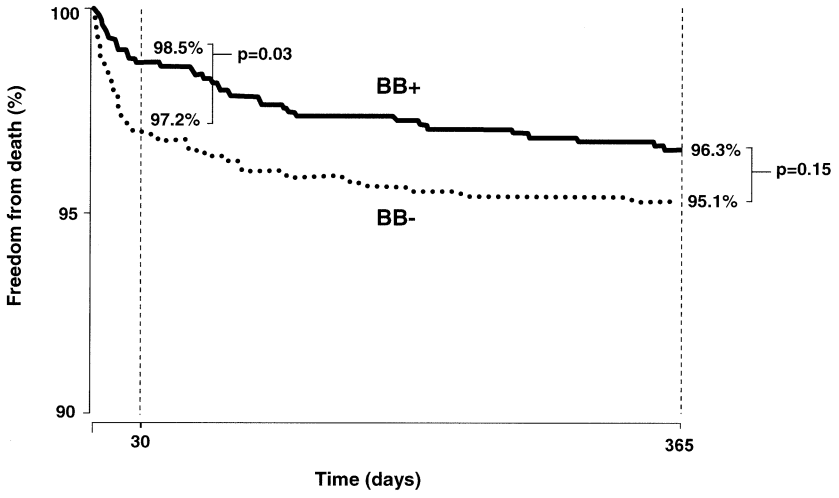

Figure 1. Freedom from death among patients treated (BB+, **solid line**) or not treated (BB−, **broken line**) with pre-procedural intravenous beta-blockers before percutaneous coronary intervention. BB = beta-blocker.

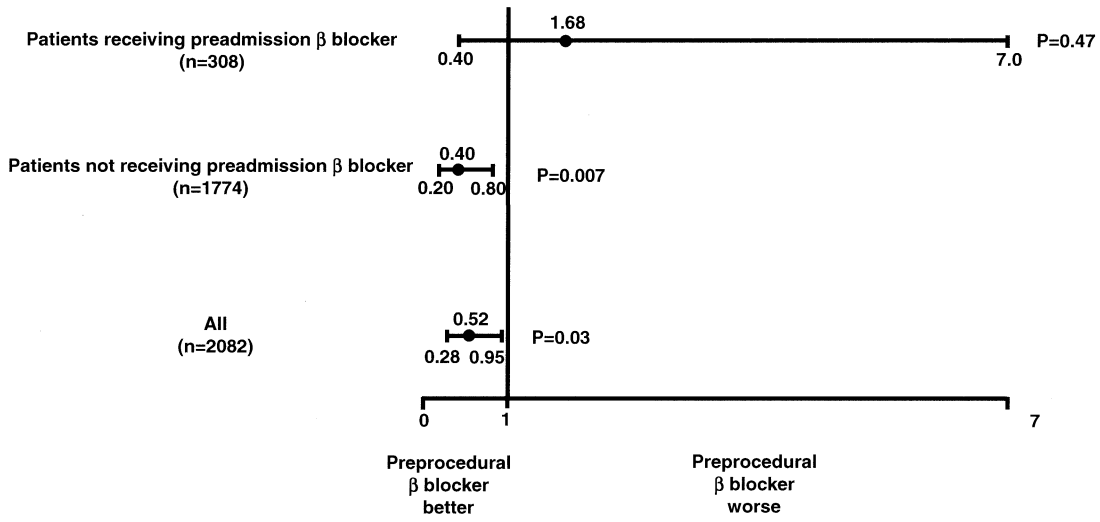

Figure 2. Hazard ratios for 30-day mortality in CADILLAC patients with respect to oral beta-blocker medication use before acute myocardial infarction, stratified by pre-percutaneous coronary intervention intravenous beta-blocker administration.

(HR = 0.42 [95% CI 0.18 to 0.96], p = 0.04) but not in those receiving previous oral beta-blocker therapy (HR = 0.76 [95% CI 0.27 to 2.13], p = 0.60).

Similarly, among patients untreated with oral beta-blockers before admission, the recovery in LVEF was greater in BB+ patients than in BB− patients (5.4% [95% CI 2.8 to 13.3] vs. 2.3% [95% CI 5.4 to 7.8], p = 0.01). In patients taking beta-blockers before admission, the change in LVEF was similar in BB+ and BB− patients (−1.2% [95% CI −4.6 to 6.5] vs. −0.5% [95% CI −7.4 to 2.0], p = 0.77). By linear regression, pre-procedural intravenous beta-blocker administration remained an independent predictor of a greater increase in LVEF from baseline to follow-up in patients not receiving oral beta-blockers before admission (beta coefficient = 3.20, p = 0.01).

DISCUSSION

The main findings of the present study are as follows: 1) pre-procedural administration of intravenous beta-blockers in patients with AMI treated by contemporary primary PCI strategies resulted in reduced mortality and enhanced recovery of left ventricular function; and 2) these benefits were confined to patients who were not maintained on oral beta-blocker therapy before admission.

Table 3. Multivariate Predictors of 30-Day Mortality Stratified by Pre-Admission Beta-Blocker Use

	Hazard Ratio (95% CI)	p Value
No pre-admission beta-blocker use		
Hypercholesterolemia	0.24 (0.07, 0.80)	0.02
Pre-procedural beta-blocker therapy	0.38 (0.17, 0.87)	0.02
Killip class 2 or 3	2.77 (1.21, 6.34)	0.02
Hypertension	3.70 (1.53, 8.97)	0.004
Renal failure (CrCl <60 ml/min)	4.41 (1.97, 9.86)	0.0003
Infarct vessel = left anterior descending	4.64 (1.92, 11.19)	0.0006
Pre-admission beta-blocker use*		
Pre-procedural beta-blocker therapy	1.68 (0.40, 7.02)	0.47

*No significant variables were identified.
CI = confidence interval; CrCl = creatinine clearance.

Impact of beta-blocker use before admission. The results of the present study confirm the survival advantage conferred by pre-procedural intravenous beta-blocker administration in patients with AMI undergoing primary PCI previously reported by the PAMI investigators (7). The current analysis importantly extends these findings, however, by identifying a strong interaction between pre-admission oral beta-blocker therapy and the efficacy of pre-procedural intravenous beta-blockers in terms of reducing mortality and enhancing myocardial recovery. We hypothesized that patients unprotected at the time of AMI onset by long-term oral beta-blocker therapy would derive the greatest clinical benefit from intravenous administration of these agents before PCI. Indeed, in this group of patients, but not in patients who had been receiving oral beta-blockers before hospitalization, pre-procedural intravenous beta-blockade resulted in a significant reduction in 30-day mortality. The absolute mortality reduction in this group at 30 days was 1.7%, corresponding to 59 patients needing to be treated in order to save one life. This absolute increase in survival was largely maintained over one year (1.2%), though with incremental mortality over time in both groups the association was no longer of statistical significance.

Baseline LVEF determined by left ventriculography at the time of PCI was lower in BB+ compared with BB− patients, possibly owing to selection bias (treatment of sicker patients with intravenous beta-blockers). The degree of LVEF recovery from baseline to follow-up was greater in the BB+ group, however, such that follow-up LVEF was comparable in both groups. As previous studies during evolving AMI have shown that LVEF is not depressed immediately after intravenous beta-blockers (12,13), the enhancement of myocardial recovery by the administration

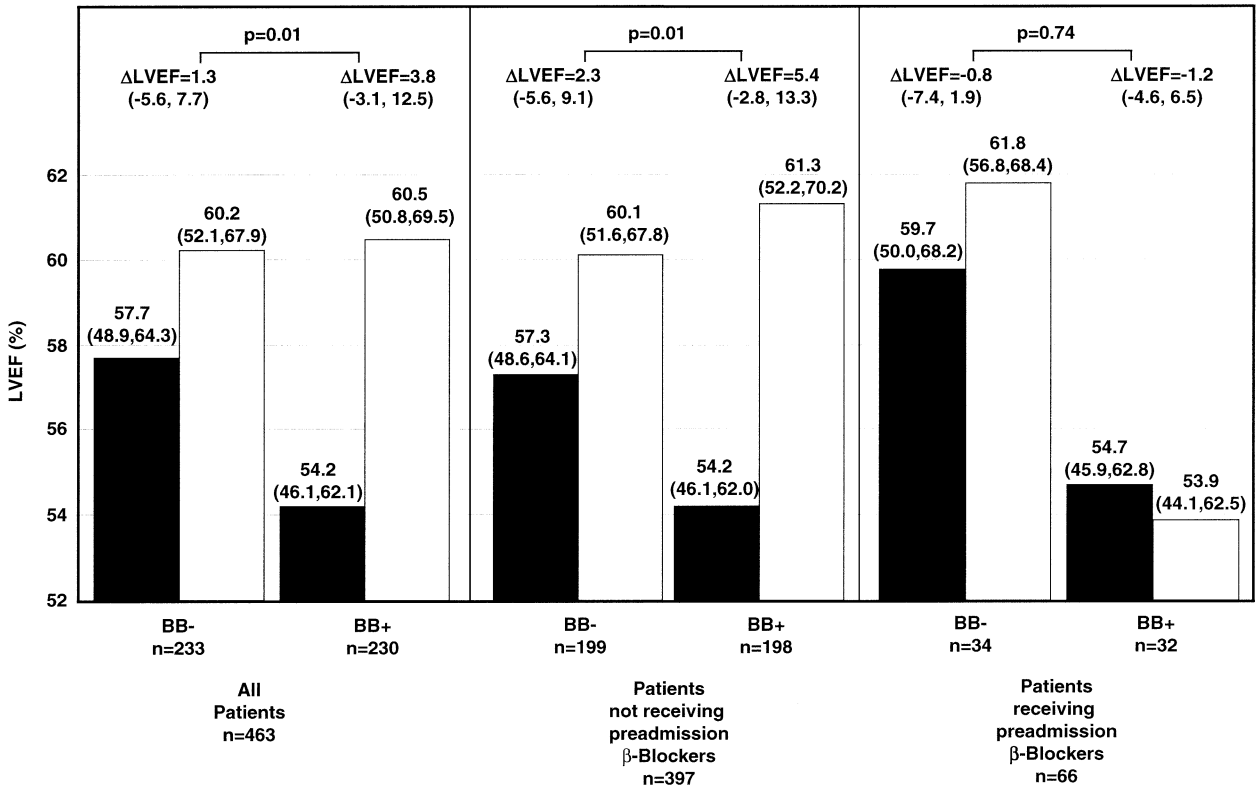

Figure 3. Change in left ventricular ejection fraction (ΔLVEF) from baseline to seven-month follow-up among patients with paired ventriculograms. BB+ **(solid bars)** and BB− **(open bars)** denote patients treated or untreated with pre-procedural beta-blockers, respectively. **Solid bars** = index LVEF. **Open bars** = follow-up LVEF.

of intravenous beta-blockers is unlikely be explained by artificial suppression of systolic function. Similar to the effect on survival, the incremental recovery in LVEF with pre-procedural beta-blockers compared with no such therapy was confined to patients previously untreated with oral beta-blockers. In this group, pre-procedural intravenous beta-blocker use was an independent predictor of global myocardial recovery from baseline to seven months. To our knowledge, the enhanced recovery in LVEF with pre-reperfusion intravenous beta-blocker use has not previously been described.

Previous studies of early beta-blockade in AMI. Previous analyses of the effect of beta-blocker administration during the early phases of AMI on survival have resulted in varying conclusions, depending on the use and type of reperfusion therapy. In the First International Study of Infarct Survival (ISIS-1) trial, conducted in the era preceding reperfusion therapy, intravenous atenolol followed by one week of oral therapy reduced in-hospital mortality by 15% in more than 16,000 enrolled patients (1). A meta-analysis confirmed the benefit of intravenous beta-blockers in reducing early mortality in the pre-thrombolytic era (14). However, randomized trials of intravenous beta-blocker administration in patients treated with thrombolytic therapy failed to demonstrate a salutary effect on survival (3–5). Indeed, a retrospective analysis of the Global Utilization of Streptokinase and TPA (alteplase) for Occluded Coronary Arteries (GUSTO-I) trial actually suggested that intravenous atenolol might increase mortality (6). Conversely, in the PAMI trials, beta-blocker use preceding primary PCI was associated with improved in-hospital survival (7). Similarly, in the present study, pre-procedural administration of intravenous beta-blockers was associated with reduced mortality at 30 days, a reduction that first became significant during the index hospitalization. By multivariate analysis, pre-procedural intravenous beta-blocker use in patients not previously maintained on oral beta-blockers was an independent predictor of survival, suggesting a possible causative relationship.

The mechanisms through which pre-procedural intravenous beta-blockers may reduce mortality in patients with AMI not maintained on oral beta-blocker therapy undergoing primary PCI are unknown. Unlike the findings reported by the PAMI trialists (7), potentially lethal procedural complications such as arrhythmias or the need for intra-aortic balloon counterpulsation were not reduced by pre-procedural beta-blockade in the present study. A possible alternative mechanism might be a reduction in infarct size with beta-blocker administration (15,16). Some studies (17,18), but not all (19), have found that oral or intracoronary beta-blocker use before elective PCI attenuates procedure-related myonecrosis. The greater extent of myocardial recovery occurring in patients pre-treated with intravenous beta-blockers in the present study supports this possibility. Less obvious is why such an effect would be

confined to patients not recently exposed to beta-blockers, though alterations in myocardial expression of beta-adrenoreceptors might be a possible explanation (20–22). The propensity for patients receiving pre-procedural intravenous beta-blockers to be discharged while receiving statins, angiotensin-converting enzyme inhibitors, and oral blockers might also contribute to enhanced late outcomes, though most of the benefit of intravenous beta-blockade in reducing mortality was seen before discharge, and by multivariate analysis in this study, discharge use of these agents was not an independent determinant of late survival.

Study limitations. The decision to use intravenous beta-blockers was not randomized, and the present analyses (including the pre-admission oral beta-blocker stratification) were post hoc. These findings must therefore be considered hypothesis-generating rather than definitive. However, pending the performance of a randomized trial investigating the role of pre-procedural intravenous beta-blockade in primary PCI, these data from a large patient population collected in a carefully controlled study provide relevant clinical evidence. Moreover, the benefit of pre-procedural beta-blockers in reducing mortality and enhancing myocardial recovery in patients not admitted while receiving oral beta-blocker therapy persisted when patients in whom beta-blocker therapy was contraindicated, including those with profound hypotension and severe bradyarrhythmias, were excluded from the analysis. The fact that no independent correlates of survival were identified in patients admitted while receiving oral beta-blockers is most likely due to the relatively small size of this group (n = 308). The applicability of our findings to patient populations under-represented in CADILLAC (e.g., octogenarians) is unknown. Lastly, the specific beta-blockers and precise doses used were not analyzed, and thus recommendations regarding the optimal pre-procedural beta-blockade regimen cannot be made.

Clinical implications. The present study supports the routine administration of intravenous beta-blocker therapy in patients with AMI not maintained on oral beta-blockers before primary PCI, in the absence of absolute contraindications, and emphasizes that such therapy may improve survival and enhance myocardial recovery in these patients. These results should not, however, be construed to suggest that patients maintained on oral beta-blocker medication be denied intravenous beta-blockers before primary PCI, especially in those with a "hyperdynamic" state, including hypertension and/or tachycardia (23). Notably, nearly half the patients in CADILLAC were not prescribed intravenous beta-blockers despite protocol recommendations. Although detailed explanations as to why beta-blockers were withheld were not collected, it is unlikely that strict contraindications were present in most patients. It is well known that beta-blockers are frequently under-prescribed in the peri-infarct period (24,25), possibly reflecting physicians' concerns about their safety in the AMI setting and misconceptions regarding absolute versus relative contraindications (26). In the present study, intravenous beta-blocker administration was safe, being associated only with a slight increase in the incidence of transient peri-procedural heart failure, without increases in adverse events such as bradyarrhythmias or severe hypotension. This safety profile, coupled with the potential benefits of enhanced survival and myocardial recovery, reinforce the importance of the administration of pre-procedural intravenous beta-blockers to most patients with AMI before primary PCI, especially those not maintained on oral beta-blocker therapy at the time of admission.

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